Adverse drug reactions of antipsychotics in frail older patients

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How to recognize and measure side effects in antipsychotic users?

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Rating scales to measure side effects of antipsychotic medication: a systematic review

Abstract

Introduction: Many patients experience side effects during treatment with antipsychotics. This article reviews the clinical use and psychometric characteristics of rating scales used to assess side effects in patients treated with antipsychotics.

Methods: A systematic literature search was performed using the electronic databases PubMed and Embase, with predefined search terms.

Results: In total 52 different scales were used in the 440 articles retrieved. For multiple side effects measured with one scale, the Udvalg for Kliniske Undersøgelser Side Effects Rating Scale for Clinicians (UKU-SERS-Clin) was used the most, whereas the Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS) had the best psychometric characteristics (Cronbach's α 0.81 and test-retest reliability 0.89). The Simpson Angus Scale (SAS) was used the most to rate extrapyramidal side effects, although the Maryland Psychiatric Research Center scale (MPRC scale) had the best characteristics (Cronbach's α 0.80, test-retest reliability 0.92 and inter-rater reliability 0.81-0.90). The Arizona Sexual Experience Scale (ASEX) was used the most to assess sexual dysfunction, but the Antipsychotics and Sexual functioning Questionnaire (ASFQ) and the Nagoya Sexual Functioning Questionnaire had the best characteristics.

Conclusion: This review will help researchers and clinicians make a purpose-oriented choice of which scale to use

Systematic review registration number: CRD42014013010.

Introduction

Antipsychotics are used worldwide for the treatment of schizophrenia, delirium, and the neuropsychiatric symptoms of dementia.[1] Unfortunately, many patients experience side effects during treatment, which may result in an impaired quality of life and early treatment discontinuation.[2,3] About half of the patients with schizophrenia experience one or more side effects.[4] The side effects of antipsychotic use for delirium have not been studied systematically,[5] but nearly half of a group of elderly patients using haloperidol, experienced parkinsonism.[6] Rating scales have been developed to evaluate the side effects of antipsychotics, such as extrapyramidal symptoms, sedation, weight gain, and sexual dysfunction.[7] However, these scales mostly evaluate a single side effect, for example parkinsonism[8] or sexual functioning,[9] and are often used for drugs other than antipsychotics alone, such as the rating scales for drug-induced parkinsonism.[8] There have been few studies of scales evaluating multiple side effects, although the use of one scale instead of several separate scales can have advantages (e.g., less time consuming) and might provide a better insight into the overall side effect profile. Lastly, rating scales can be divided into those for use in research and those for use in daily clinical practice. While psychometric characteristics are of major importance in a research setting and usability is of secondary importance, ease of use is important in a clinical setting.[7]
To date, there has been no clear review of rating scales, and their psychometric characteristics, used to assess the side effects of antipsychotics. This article reviews the clinical use and psychometric characteristics of rating scales for evaluating the side effects of antipsychotics.

Methods

This systematic review was performed using the PRISMA guidelines for systematic reviews and meta-analysis.[10] The protocol was registered under PROSPERO registration number: CRD42014013010.

Eligibility of articles

Articles describing rating scales for antipsychotic-induced side effects, written in English and Dutch, were considered eligible.

Data sources and search strategy

The databases PubMed and Embase were searched on 17 July, 2014 without limits. The search syntax used is depicted in Figure 1. All duplicate articles were excluded and the remaining articles were screened consecutively for title, abstract, and full text. If an abstract was not available, the full text of the article was screened. If the full-text article was not retrievable from the corresponding author or from national university libraries, the article was excluded. The references of the included articles were checked, in a snowball search.

Figure 1. Search syntax in Pubmed.

Pubmed [title/abstract]	Scale OR instrument
AND	
Pubmed [title/abstract]	drug induced OR adverse drug reaction OR adverse drug OR side effect OR adverse drug event OR adverse effect
AND	
Pubmed [title/abstract]	antipsychotic OR neuroleptic

Equal search strategy in Embase. No limits were used

Study selection

First, all titles were screened for relevance. The following exclusion criteria were used: (a) animal studies or non-human studies, (b) articles about children, (c) articles not about antipsychotics, (d) no rating scale discussed (if there was doubt about whether a rating scale was used, the article was not excluded) (e) articles not about adverse events or side effects, (f) side effect that was not measurable with a questionnaire or rating scale, e.g. prolonged QTc time is only measurable with an electrocardiogram (ECG), which we do not consider a rating scale. Second, the abstracts of selected articles were screened and articles were excluded with the same exclusion criteria as mentioned above and (g) a scale to measure side effects in antipsychotics was not used. Third, all possibly relevant articles were screened using the following exclusion criteria: (a) article not about adverse event scale in adults, (b) only congress abstract available, (c) full text not available, (d) language other than English or Dutch, (e) review not about side effect scales. The references of the included articles were then searched for additional articles, which were then screened as above.

The reviewers (AvS, CK) reached consensus on the eligibility of the studies after discussion based on the above eligibility and exclusion criteria.

Data extraction

Two authors (AvS and CK) independently extracted data on the number of times a rating scale was used and its psychometric characteristics. If the focus of the study was on the psychometric characteristics of the scale, the article was considered a validation study. Articles in which a rating scale was used, were considered application studies.

Strategy for data synthesis

The rating scales were classified as multidomain when multiple side effects were assessed and as single domain when only extrapyramidal symptoms or only sexual dysfunction was assessed. In the application studies, the number of times the scales were used was counted for each scale. Data from the validation studies were used to distil the psychometric characteristics of the rating scales. No additional and/or meta-analyses were performed.

Validation studies describing psychometric characteristics

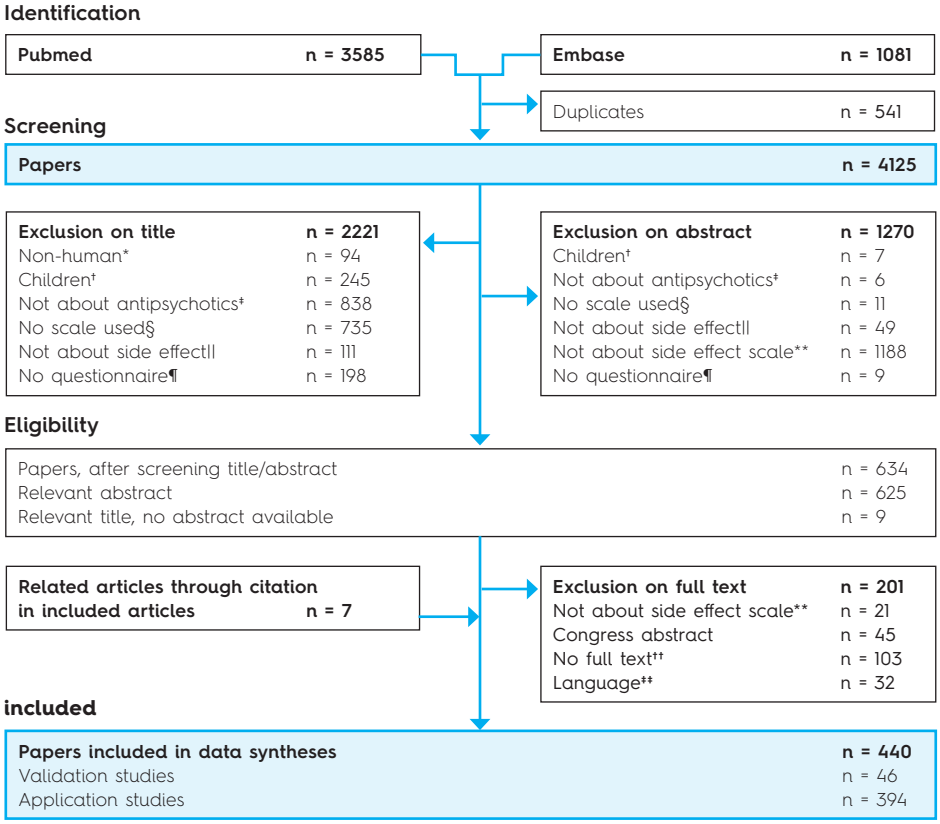
Psychometric characteristics are described in terms of reliability and validity. Reliability can be expressed in terms of internal consistency, inter-rater reliability, and test-retest reliability. Internal consistency was assessed with Cronbach's alpha, which identifies which items contribute to overall reliability, since each and every item in a rating scale has to be individually assessed for variability. Cronbach's alpha values of 0.60–0.70 were considered acceptable and values higher than 0.70 as good.[11] Inter-rater reliability and test-retest reliability or intra-rater reliability can be measured with Pearson's correlation coefficient r, Spearman's rho (ρ), intra-class correlation coefficient (ICC), or Kappa (κ). These are all correlation coefficients and a single value can be calculated to express the relationship. There is no general agreement about how to interpret the different indices of correlation and degrees of agreement. Values of 0.40–0.70 were considered to reflect a moderate correlation and values higher than 0.70 as a high correlation.[12] Validity can be expressed in terms of face validity, content validity, construct validity, convergent validity, divergent validity, and predictive validity, using correlation coefficients, as described above. Construct and convergent validity were considered sufficient if the correlation coefficient was higher than 0.70; correlation coefficients of less than 0.40 were considered to be sufficient for divergent validity.[13]

Results

Search results

Figure 2 shows the flowchart of the review. Of the 4666 articles retrieved, 440 described an antipsychotic side effects scale. Of these 440 articles, 46 articles reported the psychometric characteristics of the scale and the other 394 articles reported the use of the scale.

Figure 2. Search results with reasons for exclusion



** Exclusion criteria: *Animal studies or non-human studies †Articles about children or adolescents ‡Articles not about antipsychotics §Articles not about a rating scale ‖Articles not about side effects ¶Articles about side effects not measurable with a questionnaire **Articles that report using a scale and articles report side effect, but not a scale about side effects ††No full text = not available in full text for screening, despite all efforts, and thus excluded. ‡‡Language = language other than English or Dutch*

Table 1. Frequency of application and validation of rating scales

	Rating scale	Application studies	Validation studies
Combined side effects	Udvalg for Kliniske Undersøgelser Side Effects Rating Scale for Clinicians (UKU-SERS-Clin)	65	1
	Liverpool University neuroleptic side effect rating scale (LUNSERS)	13	3
	Matson Evaluation of Drug Side effects (MEDS)	3	1
	Association for Methodology and Documentation in Psychiatry psychotropic side effect rating scale (AMDP-5)	3	0
	Antipsychotic Non-Neurological Side Effects (ANNSERS)	2	2
	Udvalg for Kliniske Undersøgelser Side Effects Rating Scale for Patients (UKU-SERS-Pat)	1	2
	Distress Scale for Adverse Symptoms	1	0
	Subjective Side Effect Scale	1	0
	Global Index of Safety (GIS)	0	2
	Approaches to Schizophrenia Communication (ASC)	0	1
	Glasgow Antipsychotic Side effect Scale (GASS)	0	1
	Subjects Response to Antipsychotics (SRA)	0	1
	Systematic monitoring of Adverse events Related to TreatmentS (SMARTS)	0	1
	Tolerability and Quality of Life (Tool questionnaire)	0	1
Extra pyramidal side effects	Simpson-Angus Scale (SAS)	128	3
	Abnormal Involuntary Movements Scale (AIMS)	117	2
	Barnes Akathisia Rating Scale (BARS)	77	3
	Extrapyramidal Symptom Rating Scale (ESRS)	62	1
	Unified Parkinson's Disease Rating Scale	28	0
	Drug Induced Extrapyramidal Symptoms Scale (DIEPSS)	27	1
	Hillside Akathisia Scale	6	0
	Rockland Simpson Dyskinesia Scale	5	0

Table 1. Continued

	Rating scale	Application studies	Validation studies
Extra pyramidal side effects	St. Hans Rating Scale for extrapyramidal syndromes	4	1
	Abnormal Kinetic Effects Scale (TAKE)	2	0
	Dyskinesia Identification System Condensed User Scale (DISCUS)	2	2
	Mindham	1	1
	Akathisia Scale	1	0
	Australian Survey of Chan for parkinsonism	1	0
	Colombia University Rating Scale	1	0
	Cornell University Rating Scale for parkinsonism	1	0
	Dimascio Extrapyramidal Symptom Scale	1	0
	KLAWANS scale for extrapyramidal symptoms	1	0
	PERG survey for parkinsonism	1	0
	Rating Scale for Extrapyramidal Side Effects (unpublished)	1	0
	Tardive Dyskinesia Rating Scale	1	0
	SADIMOD	0	3
	Akathisia Ratings of Movement Scale (ARMS)	0	1
	Consistency Across Methods of Preference Assessment (CAMPA)	0	1
	Long instrument for diagnosis of drug induced akathisia	0	1
	Maryland Psychiatric Research Center scale (MPRC scale)	0	1
	Prince Henry Hospital Akathisia Rating Scale	0	1
	Tardive Dyskinesia Videotape Rating Techique	0	1
	Yale Extrapyramidal Symptom Scale (YESS)	0	1
	Arizona Sexual Experience Scale (ASEX)	9	2
	Psychotropic Related Sexual Dysfunction Questionnaire (PRSexDQ)	2	1

Table 1. Continued

	Rating scale	Application studies	Validation studies
Sexual dysfunction	Derogatis Interview for Sexual Function (DISF-SR)	1	0
	Sexual Function Questionnaire (SFQ)	1	0
	Changes in Sexual Function Questionnaire-14	0	1
	Antipsychotics and Sexual functioning Questionnaire (ASFQ)	0	1
	Nagoya Sexual Function Questionnaire (NSFQ)	0	1
Other single side effects	Epworth Sleepiness Scale (ESS)	2	0
	International Restless Legs Scale (IRLS)	1	0
	Food Craving Inventory	1	0
	Total	600*	46

**Some studies described more than one rating scale.*

Use of rating scales

In total, 14 rating scales for multi-domain side effects, 29 for extrapyramidal side effects, 7 for sexual dysfunction, and 3 for other single-domain side effects were used (Table 1). The Udvalg for Kliniske Undersogelser Side Effects Rating Scale for Clinicians (UKU-SERS-Clin) and the Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS) were used the most often to assess multi-domain side effects. The Simpson-Angus Scale (SAS), the Abnormal Involuntary Movements Scale (AIMS), and the Barnes Akathisie Rating Scale (BARS) were used the most often to assess extrapyramidal side effects. The scales for sexual dysfunction and the other single domain scales were not used very often in the retrieved studies.

Psychometric characteristics

The psychometric characteristics of some of the scales were not available. For example, the UPDRS was used 28 times to measure the extrapyramidal side effects of antipsychotics, but the psychometric properties of the scale for this specific goal have not been established, and the scale has been validated in patients with Parkinson's disease only. Psychometric characteristics

were available for 11 scales that measure multi-domain side effects, 16 scales that measure extrapyramidal side effects, and 5 scales that measure sexual functioning in patients using antipsychotics (Table 2). Of the multi-domain side effect scales, the UKU-SERS-Pat, the LUNSERS the Glasgow Antipsychotic Side effect Scale (GASS), and the UKU-SERS-Clin had moderate to good reliability and acceptable validity (Cronbach's α >0.70). The UKU-SERS-Clin had an intra-class coefficient of 0.49-0.91. These scales differ in the number of items scored, the time taken to complete the scale, and the rater (clinician or patient). If the patient scores the scale, there is no inter-rater reliability. The GASS takes 5 minutes to complete and grades not only the frequency of an experienced side effect but also the distress it causes.[14] The test-retest reliability (or intra-rater reliability) of the GASS was 0.72. The LUNSERS and the UKU comprehensively assess most antipsychotic-induced side effects. The "red herring" scale of the LUNSERS identifies patients who may be over-reporting symptomatology. Although some of the red herring items are obscure, for example 'chilblains'.[15] The ANNSERS was originated for the side effects of atypical antipsychotic drugs, not the conventional variety.[16,17]

Of the scales assessing extrapyramidal side effects, the SAS, the Drug Induced Extrapyramidal Symptom Scale (DIEPSS), the Maryland Psychiatric Research Center Scale (MPRC), the St. Hans Rating Scale for extrapyramidal symptoms, and the Schedule for the Assessment of Drug-Induced Movement Disorders (SADIMOD) all had good reliability and an acceptable validity (Cronbach's α>0.70; intra-rater and inter-rater reliability >0.70). The SADIMOD has never been used in other studies.

Of the sexual dysfunction scales, the Antipsychotics and Sexual Functioning Questionnaire (ASFQ) and the Nagoya Sexual Functioning Questionnaire had the best psychometric characteristics (Cronbach's α>0.70; intra-rater and inter-rater reliability about 0.70).

Table 2. Comparison of rating scales to measure side effects of antipsychotics

	Study characteristics				
	Scale	Number of items	Time to complete (min)	Self or clinician rated	Number of participants in validation study
Combined side effects	Antipsychotic Non-Neurological Side Effects (ANNSERS)[17]	39	30	Clinician and self	36
	(ANNSERS)[16]				26
	Approaches to Schizophrenia Communication (ASC)[18]	17	10	Self or Clinician	-
	Glasgow Antipsychotic Side effect Scale (GASS)[14]	22	5	Self	50
	Global Index of Safety (GIS)[19]	94	60	Clinician	2987
	(GIS)[20]				2949
	Liverpool University neuroleptic side effect rating scale (LUNSERS)[21]	51	5-20	Self	50
	(LUNSERS)[22]				83
	(LUNSERS)[15]				29
	Matson Evaluation of Drug Side effects (MEDS)[23*]	90	60	Clinician	66
	Subjects Response to Antipsychotics (SRA)[24]	74	15-20	Self	320
	Systematic monitoring of Adverse events Related to TreatmentS (SMARTS)[7]	11	5	Self	-
	Tolerability and Quality of Life (Tool questionnaire)[25]	8	5	Self	243
	Udvalg for Kliniske Undersogelser Side Effects Rating Scale for Clinicians (UKU-SERS-Clin)[26]	48	30	Clinician	2391
	Udvalg for Kliniske Undersøgelser Side Effects Rating Scale for Patients (UKU-SERS-Pat)[27]	48	11.6	Self	93
	(UKU-SERS-Pat)[28]				63

	Reliability			Validity
	Internal consistency	Test retest reliability/intra-rater reliability	Inter-rater reliability	Construct validity compared to …
	-	-	κ = 0.77 version 1 = 0.72 version 2	
	-	-	-	ρ = DISF-SR -0.273
	-	-	-	-
	α = 0.72	κ =0.72	-	ρ =LUNSERS 0.93
	-	r= 0.99	-	ρ = EUROPA vs EFESO study 0.99
	-	-	-	
	α = 0.89	r= 0.81	NA	ρ = UKU 0.82
	-	-		ρ = SAS 0.28; BARS 0.27
	-	-		ρ = UKU 0.58
	α = 0.82	-	r = 0.99	ρ = ARMS 0.85-1.00
	α = 0.69-0.93	r= 0.39-0.83	-	ρ = DAI 0.50 ρ = SWN 0.18
	-	-	-	-
	α = 0.92	-	NA	ρ = UKU -0.35 ρ = EQ-5D 0.69
	Icc = 0.49-0.92	-	-	-
	-	ρ= 0.89	NA	ρ =UKU SERS Clin 0.80
		-		ρ =UKU SERS Clin 0.46
	-		NA	

Table 2. Continued

		Study characteristics			
	Scale	**Number of items**	**Time to complete (min)**	**Self or clinician rated**	**Number of participants in validation study**
Extrapyramidal side effects	Abnormal Involuntary Movements Scale (AIMS)[29]	10	10	Clinician	16
	(AIMS)[30]				-
	Akathisia Ratings of Movement Scale (ARMS)[23]	7	10	Clinician	66
	Barnes Akathisia Rating Scale (BARS)[31]	4	10	Clinician and self	42
	(BARS)[32]				-
	(BARS)[33]				99
	Consistency Across Methods of Preference Assessment (CAMPA)[34]	3	-	Clinician	63
	Drug Induced Extrapyramidal Symptoms Scale (DIEPSS)[35]	9	-	Clinician	182
	Dyskinesia Identification System Condensed User Scale (DISCUS)[36]	34	-	Clinician	36
	(DISCUS)[37]				216
	Extrapyramidal Symptom Rating Scale (ESRS) [38]	45	15	Clinician	374
	Long instrument for diagnosis of drug induced akathisia[39]	16	-	Clinician	360
	Maryland Psychiatric Research Center scale (MPRC scale)[40]	31	-	Clinician	1107
	Mindham[41]	9	-	Clinician	-
	Prince Henry Hospital Akathisia Rating Scale[42]	10	-	Clinician	100
	SADIMOD[43]	34	30	Clinician	31
	SADIMOD[44]				31
	SADIMOD[45]				-

	Reliability			Validity
	Internal consistency	Test retest reliability/ intra-rater reliability	Inter-rater reliability	Construct validity compared to …
	Icc = 0.05-0.29	-	-	-
		-	-	-
	α = 0.67	-	r = 0.69	ρ = 0.66-1.00
	-	-	κ = 0.74-0.95	-
				ρ = DIEPSS 0.88-0.97
	-	-	-	ρ = SADIMOD 0.57-0.88
	-	-	-	ρ = Lower limb activity index 0.26
	-	-	-	-
	-	r = 0.6-0.91	icc 0.76-0.96	ρ = SAS, BARS, AIMS 0.88-0.97
	-	-	-	-
	α = 0.92	-	r = 0.45-0.93	-
	-	-	r = 0.80-0.97	ρ = AIMS 0.96
	-	-	-	-
	α = 0.80	r = 0.92	r = 0.81-0.90	ρ = AIMS 0.97
	-	-	-	-
	α = 0.90	-	κ = 0.42-0.81	ρ = BARS 0.84
	α = 0.75-0.94	r = 0.33-0.77	-	ρ =SAS, BARS, AIMS 0.57-0.88
	α = 0.81-0.94	-	r = 0.46-0.71	-
	-	-	-	

Table 2. Continued

		Study characteristics			
	Scale	**Number of items**	**Time to complete (min)**	**Self or clinician rated**	**Number of participants in validation study**
Extrapyramidal side effects	Simpson-Angus Scale (SAS) [46] (SAS) [47] (SAS) [48]	10	10	Clinician	14 99 15
	St. Hans Rating Scale for extrapyramidal syndromes[49]	21	-	Clinician	30
	Tardive Dyskinesia Videotape Rating Techique[50]	24	-	Clinician	94
	Yale Extrapyramidal Symptom Scale (YESS)[51]	8	-	Clinician	63
Sexual dysfunction	Antipsychotics and Sexual functioning Questionnaire (ASFQ)[52]	M 7/ F 9	5	Clinician	30
	Arizona Sexual Experience Scale (ASEX)[53] ASEX[54]	5	5	Self or clinician	247 165
	Changes in Sexual Function Questionnaire-14 [55]	14	10	Self or clinician	171
	Nagoya Sexual Function Questionnaire (NSFQ)[56]	7	5	Self	60
	Psychotropic Related Sexual Dysfunction Questionnaire (PRSexDQ)[57]	7	5	Clinician	45

*α= Cronbach's alpha, icc= intraclass correlation coefficient, ρ= Spearman's rho, r= Pearson's r, κ = Cohen's kappa, - = not described in the article NA= Not applicable, there is no inter-rater reliability in self administered scales M= male subjects, F= female subjects *In this article only the Central Nervous System Items of the MEDS were used and validated. SWN=-Subjective Wellbeing under Neuroleptics, DAI= Drug Attitude Inventory, SmPC=Summaries of Product Characteristics, CGI-SF= Clinical Global Impression - Sexual Functioning, BISF= Brief Index of sexual functioning.*

	Reliability			Validity
	Internal consistency	Test retest reliability/ intra-rater reliability	Inter-rater reliability	Construct validity compared to ...
	-	-	r = 0.71-0.96	-
	α = 0.79	-	-	-
	α = 0.83	-	r = 0.71-0.85	ρ = SADIMOD 0.66
	α = 0.82	r = 0.66-0.85	r = 0.79	ρ = AIMS 0.50
	-	r = 0.82-0.96	r = 0.83-0.99	ρ = AIMS 0.63
	-	-	κ = 0.65-0.80	ρ = Websters items 0.74-0.91
	α = M 0.84	r = 0.76	r = 0.61-0.84	ρ = SRA 0.54-0.98 ρ = ASEX 0.16-0.71
	α = 0.90	-	-	
	α = 0.90	-	-	BISF "good validity"
	α = 0.90	-	-	ρ = VAS-SFS 0.33 ρ = CGI-SDS 0.71
	α = M 0.76 α = F 0.79	r = M 0.92 r = F 0.92	NA	UKU M r = 0.69 F r = 0.85
	α = 0.68	-	-	ρ = CGI-SF 0.729

Discussion

Several rating scales are available to assess the side effects of antipsychotics, some of which assess multiple or multi-domain side effects whereas others assess single effects, such as extrapyramidal symptoms or sexual functioning. The UKU-SERS-Clin was used the most to assess multi-domain side effects, whereas the LUNSERS had the best psychometric characteristics (Cronbach's α 0.81 and test-retest reliability 0.89). The SAS was used the most to assess extrapyramidal side effects, but the MPRC had the best characteristics (Cronbach's α 0.80, test-retest reliability 0.92 and inter-rater reliability 0.81-0.90). The ASEX was used the most to assess sexual dysfunction, but the ASFQ and the Nagoya Sexual Functioning Questionnaire had the best characteristics. We found a discrepancy between the scales used and the scales validated for a particular use – most (n=21) of the scales used did not have psychometric characteristics for the population investigated. On the other hand, some validated scales have never been used (n=17).

To our knowledge, this is the first study to review rating scales that assess multi-domain side effects in one rating scale. In contrast, single-domain scales are frequently used. Suzuki et al. reported that clinical trials for schizophrenia mostly use the single-domain scales AIMS, BARS, and SAS,[58] and that the UKU side effect rating scale lacks some crucial elements, such as metabolic parameters. They also reported that multi-domain scales are difficult to score.[58] Knol et al. evaluated rating scales for drug-induced parkinsonism and concluded that the SAS, St. Hans Rating Scale for Extrapyramidal Syndromes, and DIEPSS seem to be the most valid, reliable, and easy-to-use scales for use in clinical practice.[8] We also found that the SAS, BARS, and AIMS were used the most to assess extrapyramidal symptoms and that the SAS, St. Hans Rating Scale, and DIEPSS had good psychometric characteristics. We found that the MPRC had the best characteristics. De Boer et al. described the psychometric characteristics of rating scales to assess sexual functioning in patients using antipsychotics and concluded that the ASFQ, the Changes in Sexual Functioning Questionnaire-14 (CSFQ-14), and the Psychotropic-Related Sexual Dysfunction Questionnaire (PRSexDQ) cover all aspects of sexual functioning and should preferably be used for this indication.[9] We found that the ASFQ and Nagoya Sexual Functioning Questionnaire had good psychometric characteristics. Our findings are in line with those of earlier studies and provide a clear overview of multi-domain rating scales. Side effects are frequently missed, either because clinicians do not always ask about them or do not recognize complaints as possible

side effects. A rating scale in which multi-domain side effects are combined, or the combined use of multiple rating scales, can be advantageous in patient care because many patients experience multiple side effects during treatment with antipsychotics, which may result in an impaired quality of life and early discontinuation of medication.[2, 3] There can be some discrepancies between the distress associated with certain side-effects by prescribers and consumers of neuroleptic drugs and the fact that patients are unlikely to attribute symptoms as side effects of neuroleptic medication.[59] This article provides an overview of the multi-domain and single-domain side effect scales currently available and provides clinicians and researchers with goal-oriented choices. Scales that are easy to use and which take little time to complete are most appropriate for clinical use. One option is for patients to complete a scale in the waiting room before an appointment with their physician. The UKU-SERS-Pat, the LUNSERS, and the GASS can be used as self-rating scales and can serve as a starting point for a patient–clinician discussion of drug side effects and tolerability. It should be noted that potentially life threatening side effects such as neuroleptic malignant syndrome, significant QTc prolongation are also very important, although they fail to be captured with the existing rating scales. The prescribing physician should consider to base the selection on antipsychotics in light of the differences in side effects profiles, rather than those in antipsychotic efficacy. For each patient the choice of treatment has to be made individually. In contrast, research requires the use of scales with good psychometric characteristics. The MPRC had the best psychometric properties, but this scale assesses extrapyramidal side effects only. The LUNSERS and the UKU-SERS-Clin had the best psychometric characteristics of the multi-domain side effect scales; however, it should be noted that the correlation coefficient between the patient- and clinician-rated versions of the latter scale (UKU-SERS-Pat and the UKU-SERS-Clin, respectively) varied between 0.46 and 0.80 and was not very high. Patients tended to report more, and more severe side effects than clinicians did. This is probably because clinicians tend to underestimate drug-induced discomfort experienced by patients.[28] However, it is possible that patients interpret side effects in a different manner. For example, clinicians may interpret discomfort as a mood symptom, whereas patients may consider it a side effect and overstate its severity.[27, 28] For research purposes, a clinician-administered scale might be more appropriate for monitoring the side effects of antipsychotics, because it is more objective.

Although this study provides an overview of rating scales, it had some limitations. Although the literature was searched for relevant rating scales, but it should be

appreciated that the literature does not necessarily reflect clinical practice. The frequency with which a scale is actually used in daily practice can never be determined based on the literature, and thus we can only give a global indication of how often a scale is used in clinical practice and how this figure relates to the use of other scales. However, as we also performed a snowball search of the references of included articles, we believe the search provides a fairly complete picture of the scales in use. Another potential limitation is that we assumed that relevant rating scales would be published in journals included in PubMed or Embase. Moreover, we may have missed general scales about the side effects of all psychotropic drugs, but it is unlikely that these scales would have been validated in antipsychotic users. In clinical practice, it is very difficult for acute psychotic patients to fill out self-report scales, and in this instance clinician-rated scales are probably more appropriate. However, chronic users of antipsychotic medication, such as patients with schizophrenia, are capable of filling out self-report scales, and the use of such scales to assess the side effects of medication may improve patients' medication adherence and knowledge of drug side effects, which might improve their quality of life.

In summary, given the frequency and nature of antipsychotic-induced side-effects, it is essential to assess these side effects in clinical practice. The UKU-SERS-Pat, the LUNSERS, and the GASS seem to have moderate to good reliability and acceptable validity. Because these scales can be completed by patients relatively quickly, they are the most appropriate for use in clinical practice. The UKU-SERS-Clin is a comprehensive, clinician-rated scale and can be used for research purposes, because of its good psychometric characteristics. In addition to multi-domain scales, a combination of single-domain scales can probably also be used, for example, the SAS for EPS or the ASFQ for sexual dysfunction. However, the use of a combination of single-domain scales will not cover all side effect domains and the psychometric characteristics of such combinations needs to be studied in the future.

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